STATUS OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Canceled).

2. (New) A method of preferentially targeting a biologically active antisense oligonucleotide to hepatic tissues in a mammal in need of hepatic gene modulation, to modulate the expression of a gene in the liver of a mammal, comprising the step of conjugating the oligonucleotide to a cholesteryl moiety and administering the cholesterol-oligonucletide conjugate to said mammal to achieve said preferential targeting.

3. (New) A method of modulating the expression of a nucleic acid in the hepatic system of a mammal in need of hepatic gene modulation, comprising the step of administering to said mammal a compound to modulate the expression of said nucleic acid, said compound comprising a plurality of linked nucleosides, wherein:

each nucleoside includes a ribofuranosyl sugar portion and a base portion; and

at least one of said nucleosides bears at a 2'-O-position, a 3'-O-position, or a 5'-O-position a substituent having formula:

$$-R_A\text{-}N(R_{1a})(R_{1b})$$

where:

R_A is alkyl having from 1 to about 10 carbon atoms or $(CH_2\text{-}CH_2\text{-}Q)_x$;

R_{1a} and R_{1b}, independently, are H, R_2, an amine protecting group or have formula $C(X)\text{-}R_2$, $C(X)\text{-}R_A\text{-}R_2$, $C(X)\text{-}Q\text{-}R_A\text{-}R_2$, $C(X)\text{-}Q\text{-}R_2$; and

R_2 is cholesterol;

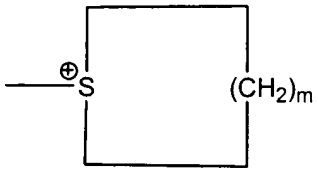
X is O or S;

each Q is, independently, NH, O, or S;

x is 1 to about 200;

R_3 is H, R_A, C(O)OH, $C(O)OR_A$, $C(O)R_4$, $R_A\text{-}N_3$, or $R_A\text{-}NH_2$;

R_4 is Cl, Br, I, SO_2R_5 or has structure:



m is 2 to 7; and

R_5 alkyl having 1 to about 10 carbon atoms;

wherein at least one of R_{1a} and R_{1b} are R_2.

4. (New) A method of preferentially targeting an oligonucleotide to hepatic tissues in a mammal in need of hepatic gene modulation, said method comprises administering to said mammal an oligonucleotide having a cholesteryl moiety conjugated thereto, to preferentially target said oligonucleotide to hepatic tissues in said mammal.

5. (New) The method of claim 4 wherein said cholesteryl moiety is conjugated to said oligonucleotide through an alkylamine tether.

6. (New) The method of claim 4 wherein said cholesteryl moiety is conjugated to said oligonucleotide at the terminal 5'-hydroxyl group of said oligonucleotide.

7. (New) The method of claim 4 wherein said cholesteryl moiety is conjugated to said oligonucleotide at the terminal 3'-hydroxyl group of said oligonucleotide.

8. (New) The method of claim 4 wherein said cholesteryl moiety is conjugated to said oligonucleotide at a 2'-hydroxyl group of said oligonucleotide.